UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/757,781	01/09/2001	Roopa Reddy	PC-0032 US	8475

27904 7590 03/16/2004

INCYTE CORPORATION
3160 PORTER DRIVE
PALO ALTO, CA 94304

EXAMINER	
RAWLINGS, STEPHEN L	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 03/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application No.	Applicant(s)	
	09/757,781	REDDY ET AL.	
	Examiner	Art Unit	
	Stephen L. Rawlings, Ph.D.	1642	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 21 August 2003 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☐ The period for reply expires _____months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☒ A Notice of Appeal was filed on *30 September 2003*. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2. ☐ The proposed amendment(s) will not be entered because:

   (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);

   (b) ☐ they raise the issue of new matter (see Note below);

   (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

   (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____.

3. ☒ Applicant's reply has overcome the following rejection(s): See Note of Explanation.

4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5. ☒ The a)☐ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: *See Note of Explanation*.

6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7. ☒ For purposes of Appeal, the proposed amendment(s) a)☐ will not be entered or b)☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

   The status of the claim(s) is (or will be) as follows:

   Claim(s) allowed: _____.

   Claim(s) objected to: _____.

   Claim(s) rejected: *1 and 3-8*.

   Claim(s) withdrawn from consideration: *9-14*.

8. ☐ The drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.

9. ☐ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). _____.

10. ☒ Other: *See attached Note of Explanation*

Note of Explanation

The amendment filed August 21, 2003 is acknowledged and has been entered. Claims 2 and 15-22 have been canceled. Claims 3 and 4 have been amended.

Entry of the amendment has obviated the following grounds of rejection the rejection of claims 3 and 4 under 35 USC § 112, first paragraph, as containing new matter, for the reasons set forth in section 9 of the Office action mailed July 2, 2003.

However, entry of the amendment filed August 21, 2003 fails to place this application in condition for allowance, because the amendment does not obviate the other rejections set forth sections 7, 8, and 11-13 in the Office action mailed July 2, 2003.

Applicant's have traversed the rejection of claims 1 and 3-8 under 35 USC § 112, first paragraph as lacking adequate written description, for the reason set forth in section 7 of the Office action mailed July 2, 2003, arguing the following:

Applicant has stated the basic argument set forth in reply to the Office action mailed December 3, 2002 is reiterated. The specification provides an adequate written description of the claimed variant of SEQ ID NO: 2 in terms of chemical and structural properties of SEQ ID NO: 2. The recitation of functional characteristics shared by at least a substantial number of members of the claimed genus of proteins is not an absolute requirement for fulfilling the written description requirement.

In addition, Applicant has submitted none of the literature cited by the Examiner, which teaches the difficulty of predicting protein function based on homology, suggests that functional homology cannot be inferred by a reasonable probability in this case. Brenner's basic rule that sequence homology in excess of 40% over 70 or more amino acid residues yields high probability of functional homology. At best, the literature cited by the Examiner stands for the proposition that it is difficult to predict the function of a protein based on sequence comparisons.

Applicant's arguments have been carefully considered but not found persuasive for the following reasons:

The Examiner reiterates the response to Applicant's arguments, which is set forth in the Office action mailed July 2, 2003 in reply to Applicant's amendment filed February 4, 2003. The written description set forth in Applicant's specification of the claimed genus of cDNA molecules is inadequate and fails to meet the written description requirement set forth under 35 USC § 112, first paragraph, because even given benefit of Applicant's disclosure, the skilled artisan could not immediately envisage, recognize, or distinguish at least a substantial number of members of the claimed genus of cDNA molecules from other cDNA molecules encoding proteins having an amino acid sequence, which is at least 90% identical to SEQ ID NO: 20 but which differs from SEQ ID NO: 20. Accordingly, Applicant's disclosure of the claimed invention would not reasonably convey to the skilled artisan that Applicant had possession of the claimed invention at the time the application was filed.

Applicant has argued the specification provides an adequate written description of the claimed variant of SEQ ID NO: 2 in terms of chemical and structural properties of SEQ ID NO: 2; however, the claims are drawn to a genus of cDNA molecules encoding structurally different proteins. The only member of the claimed genus described by Applicant is the cDNA molecule of SEQ ID NO: 20, which encodes the polypeptide of SEQ ID NO: 2, so Applicant has not met the written description requirement by describing an actual reduction to practice, or by disclosing the structures of at least a substantial number of the members of the claimed genus, and the polypeptide of SEQ ID NO: 2 is not deemed representative of at least a substantial number of members of the claimed genus. The polypeptide of SEQ ID NO: 2 is not deemed representative, because even given Applicant's disclosure of SEQ ID NO: 2, the skilled artisan could not immediately envisage, recognize, or distinguish at least a substantial number of members of the claimed genus of cDNA molecules from other cDNA molecules encoding proteins having an amino acid sequence, which is at least 95% identical to SEQ ID NO: 2 but which differs from SEQ ID NO: 2, because the specification does not describe a characteristic or particularly identifying feature of the polypeptide of SEQ ID NO: 2, which is shared by at least a substantial number of members of the claimed genus, so that the skilled artisan could recognize or distinguish the others proteins encoded by the claimed genus of proteins, which differ structurally from SEQ ID NO: 2.

In reply to Applicant's remark, the recitation of functional characteristics shared by at least a substantial number of members of the claimed genus of proteins is not an absolute requirement for fulfilling the written description requirement, Applicant is correct. As stated in the Office action mailed July 2, 2003 at page 7 and 8, *The Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, paragraph 1, ``Written Description'' Requirement* (66 FR 1099-1111, January 5, 2001) state, "[p]ossession may be shown in a variety of ways including description of an actual reduction to practice, or by showing the invention was 'ready for patenting' such as by disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention" (*Id.* at 1104).

In reply to Applicant's argument, none of the literature cited by the Examiner suggests functional homology cannot be inferred by a reasonable probability in this case, it is aptly noted Applicant later remarks, at best, the literature cited by the Examiner stands for the proposition that it is difficult to predict the function of a protein based on sequence comparisons alone. The literature establishes that sequence comparisons alone do not yield a reliable inference of a protein's function. Thus, the literature cited by the Examiner supports the Office's position that even given the disclosure of SEQ ID NO: 2, the skilled artisan could not predict, which variant of the polypeptide of SEQ ID NO: 2 having an amino acid sequence that is at least 95% identical to SEQ ID NO: 2, or which are encoded by a cDNA molecule comprising a polynucleotide sequence that is at least 90% identical to SEQ ID NO: 20 would have a function that is the same as, or similar to the function of the polypeptide of SEQ ID NO: 2. If the skilled artisan could predict which cDNA molecules comprising a polynucleotide sequence that is at least 90% identical to SEQ ID NO: 20 encode proteins that are functionally similar or identical to the polypeptide of SEQ ID NO: 2, it follows the skilled artisan cannot envisage, recognize, or distinguish members of the claimed genus and would not be reasonably persuaded that Applicant had possession of the claimed invention at the time the application was filed.

In reply to Applicant's remark, Brenner's basic rule is that sequence homology in excess of 40% over 70 or more amino acid residues yields high probability of functional homology, Brenner et al. discloses the sequence comparisons can yield reasonable inference that proteins are evolutionarily related, or that the genes encoding the proteins have evolved from a common

ancestral gene. However, Brenner et al. does not teach sequence comparisons can yield a reasonable inference that two proteins have redundant or even similar functions.

Applicant has traversed the rejection of claims 1 and 4-8 under 35 USC § 112, first paragraph as introducing new matter for the reason set forth in section 8 of the Office action mailed July 2, 2003, arguing the following:

Explicit support for the terms "naturally occurring" and "variant" is found in the specification. The combination of the terms in the term "naturally occurring variant" in the claims would be understood by one skilled in the art as referring to a variant of SEQ ID NO: 20, or a variant of SEQ ID NO: 2, which occurs in nature. The ability to combine the terms shows Applicant was in possession of such variant at the time the application was filed.

Applicant's arguments have been carefully considered but not found persuasive for the following reasons:

The fact that the term "naturally occurring variants" of SEQ ID NO: 2 or SEQ ID NO: 20 would be understood as referring to a variant of SEQ ID NO: 20, or a variant of SEQ ID NO: 2, which occurs in nature, is not disputed. However, the mere fact that the terminology is recited in the specification would not reasonably convey to the skilled artisan that Applicant had possession of the claimed "naturally occurring variants" of SEQ ID NO: 2 or SEQ ID NO: 20. While the terms "naturally occurring" and "variant" appear in the specification, the terms are not used in the context of describing the claimed "naturally occurring variants" of SEQ ID NO: 2 or SEQ ID NO: 20. As stated in the previous Office action, the disclosure at page 7, refers to derivatives of naturally occurring molecules, but does not provide explicit or implicit support for the recitation of the limitation "naturally occurring variant" in the claims. The disclosure at page 12 states, "as a result of the degeneracy of the genetic code, a multitude of cDNA encoding ARP, some bearing minimal similarity to the cDNAs of any known and naturally occurring gene, may be produced" (lines 39-41); thus, this disclosure also does not provide the necessary antecedent basis. Finally, the disclosure at page 13 refers to possible variations in the structure of a cDNA molecule encoding a polypeptide, which could be *made* by selecting combinations based on possible codon choices in accordance with the standard triplet genetic code as applied to the polynucleotide encoding naturally occurring ARP. Accordingly, the disclosure at page 13 does

not provide antecedence for the recitation of the limitation of "naturally occurring variant" in the claims.

Applicant has traversed the rejection of claim 4 under 35 USC § 102 as being anticipated by Joberty et al., Izumi et al., or NCI-CGAP for the reasons set forth in sections 11, 12, or 13, respectively, of the Office action mailed July 2, 2003, arguing the following:

The Examiner's interpretation that claim 4 be read as encompassing a plurality of nucleic acid molecules comprising a polynucleotide sequence of two or more contiguous nucleotide residues of the polynucleotide sequence set forth as SEQ ID NO: 20 is unfounded. The context of the term "a cDNA" as recited in claim 4 dictates that the claimed cDNA molecule minimally comprise the complete sequence of SEQ ID NO: 20.

Applicant's arguments have been carefully considered but not found persuasive for the following reasons:

Claim 4 is drawn to a cDNA comprising a sequence of a nucleic acid sequence of SEQ ID NO: 20, or its complement. In examining the novelty of a claim, the claim is given its broadest reasonable interpretation in light of the specification. The specification teaches, "the singular forms 'a', 'an', and 'the' include plural reference unless the context clearly dictates otherwise" (specification, page 6, lines 12 and 13). Because the nucleic acid molecule of the prior art comprises one or more sequences of the polynucleotide sequence set forth in SEQ ID NO: 20, the disclosure of the prior art is deemed anticipatory of the claimed invention. Contrary to Applicant's assertion, the Examiner's interpretation that claim 4 be read as encompassing a plurality of nucleic acid molecules comprising a polynucleotide sequence of two or more contiguous nucleotide residues of the polynucleotide sequence set forth as SEQ ID NO: 20 is *not* unfounded, as support for the Examiner's interpretation is found in the specification at page 6, lines 12 and 13. Accordingly, also contrary to Applicant's assertion, in light of Applicant's disclosure of the invention, the context of the term "a cDNA" as recited in claim 4 does *not* dictate that the claimed cDNA molecule minimally comprise the complete sequence of SEQ ID NO: 20.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen L. Rawlings, Ph.D. whose telephone number is (571) 272-0836. The examiner can normally be reached on Monday-Friday, 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne (Bonnie) Eyler, Ph.D. can be reached on (571) 272-0871. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Stephen L. Rawlings, Ph.D.
Examiner
Art Unit 1642

slr
March 4, 2004